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Introduction

The September 11, 2001, attacks against the United States and the spate of civilian anthrax casualties provided a painful wake-up call to the Nation. Clearly, U.S. adversaries do not need large armies or intercontinental missiles to threaten ordinary citizens, and asymmetrical warfare can potentially negate traditional military strengths. The Army's challenge is to use science and technology to consistently transform itself with the expanding spectrum of threats.

A recent study by the National Research Council Board on Army Science and Technology (NRC BAST), *Opportunities in Biotechnology for Future Army Applications*, examined ways that biotechnology can increase the combat effectiveness of future soldiers and systems. The study identified promising areas of research in sensors, materials, computing and electronics, logistics, and medicine. These pursuits have become all the more relevant in the months since the study was published.

Biotechnology has long been used to detect, identify, and track disease origins. Two critical roles for biological detection are force protection on the battlefield and the unambiguous identification of biological samples. This latter role is sometimes referred to as "bioforensics" because of its use in legal proceedings.

An example of bioforensics was the successful identification in 1993 of a mysterious pathogen that destroyed human lung tissue. The lethal pathogen, discovered in New Mexico, was traced to a hantavirus (isolated from striped field mice near the Hantaan River in South Korea in 1976) using polymerase chain reaction (PCR) technology. PCR uses DNA (deoxyribonucleic acid) to propagate, identify, and sequence viral genes from a victim's tissue. Along with other

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biotechnology tools, investigators use techniques similar to PCR to search for the "biological signature" of anthrax spores contained in letters sent through the U.S. mail in recent bioterrorist attacks.

Sensor Technologies

Numerous sensor technologies, based on immunoassays, nucleic acid assays, and photo-optics, use biotechnology to detect threats in the air and water. In the future, these may also be used to monitor soldiers for symptoms of exposure to harmful substances. Biochips as small as postage stamps can now perform sophisticated chemical and biological analyses on food products. A network of biosensors, perhaps integrated with field uniforms, might someday augment other sensors and intelligence sources to give commanders a more complete picture of opposing forces and provide a record of the battlefield environment.

Differences exist between Army battlefield detection requirements and commercial detection systems. To be deployable, for example, commercial biosensor systems need to be made more versatile and less reliant on biological reagents. Battlefield detection systems need to be self-contained, precise, and rugged. Other military requirements, such as miniaturization and networking of sensors, are not likely to be addressed without Army investment and encouragement.

Genomics Research

The Human Genome Project and related private efforts have paved the way for exploiting the vast amount of information coded by genes. Gene expression monitoring involves extracting data from DNA by looking at the up- and down-regulation of genes, assessing

which steps in the body's metabolic pathways are affected, and correlating this information with human characteristics. Genomics research will allow drugs, dosages, and therapies to be "tailored" to individual soldiers and may lead to scientific ways to predict behavior.

Toxicogenomics, an area closely related to genomics, involves studying correlations between gene and protein expression (e.g., immune response characteristics) and reactions to toxic agents. Genes often respond to toxic insult weeks or even months before the onset of observable pathology and at exposure levels that do not produce overt symptoms.

Toxicogenomics research can provide insight on how to detect and defend against chemical and biological warfare agents as well as toxic industrial chemicals or pathogens in foreign countries where environmental protection standards are not up to those of the United States. The NRC study recommended that the Army invest in this area of military-specific genomic research as one way of leveraging commercial genomics applications as opportunities appear on the horizon. In the far term, the study predicted that the Army should lead the way toward open, disciplined use of genomics data to enhance soldier health and performance.

But other genomics applications needed by the Army may not be addressed by the biotech industry. For example, quick-response vaccine development and small-scale vaccine production capabilities are important and clearly define Army biotechnology requirements. Commercial market incentives are lacking for both, but the mission (and market) is likely to expand with homeland defense requirements to prepare for future bioterrorist contingencies. Genomics research has opened the door to new technologies for vaccine development, and the Army should support research in such areas as engineered viruses, cell-based vaccines, DNA vaccines, and monoclonal antibodies.

Army Influence

The Army will have a difficult time influencing the course of biotechnology development. For one thing, commercial research and development is focused on agriculture, medicine, and the environment, and many important Army applications are nonmedical. Also, this emerging industry consists of a diverse assortment of a few large pharmaceutical and agricultural product companies and hundreds of small entrepreneurial ventures. The industry is highly competitive in a myriad of specialty fields, including genomics, bioinformatics, microfluidics, and nanotechnology. The dollars spent by the industry on drug research and development alone far surpass that for all Army research and development, so forging multiple partnerships for influence and leverage will be essential for the Army.

Biomaterials

The NRC BAST study found that many promising biotechnologies will result from research in biological hybrid materials and biologically inspired materials. Biomaterials compatible with the human body could start the wound-healing processes on the battlefield and accelerate the repair of bones through self-replication. Innovative tissue engineering, including the use of stem cells, could repair cartilage and replace dead or damaged tissue. However, new techniques are needed to associate protein structure with function and to optimize the design of proteins through genetic engineering.

Proteins

A growing body of knowledge about proteins, known as proteomics, is leading the way toward a multitude of important applications. For example, specific proteins that can enable growth of synthetic materials on biological surfaces may resolve biocompatibility issues and facilitate the implantation of sensors, monitors, and other microscale devices. Other benefits to the Army include protein-based electronic components, lightweight armor produced from structural protein polymers, and catalytic enzymes for the degradation of toxic materials.

The focus on proteins has already led to important developments in molecular electronics for use in electronics, computing, communications,

and power systems. Protein-based computer memories provide secure and practically limitless data storage in harsh field environments. Additionally, there is strong evidence that genetically engineered proteins can be used to make electronics components immune to radiation weapons.

Biological photovoltaic cells, mimicking natural photosynthetic processes, may provide soldiers with alternatives to batteries for radios, displays, and other field equipment. Advances in agricultural biotechnology that are enabling production of multifunctional foods, such as edible vaccines, can potentially simplify logistics support for small units. However, perhaps even more important to logistics is biological research underpinning the miniaturization of systems.

Nanotechnology

Many of the top-down advances in nanotechnology have resulted from bottom-up revelations in molecular and cellular biology. Nanoscale devices consisting of cantilevers, pumps, valves, channels, and electronic components show exciting potential to conserve power, integrate external and internal sensor systems, and perform useful functions independently in transparent modes. Nanoscale structures that mimic biological functions could be used to assess physiological status (e.g., alertness) or responses to battlefield contaminants or biological threats. Other devices might combine biological or synthetic components with silicon to accomplish sensing functions not possible by any other means.

Nanotechnology is thought to have so much potential that the government committed more than \$500 million to a National Nanotechnology Initiative and the Army has established a Soldier Nanotechnology Center where academic and Army scientists can work concurrently on common applications.

Other facets of biotechnology, including toxicogenomics, molecular electronics, and biologically inspired materials, are likely to have extraordinary impact on future Army operations. However, research is needed in several key areas to overcome critical barriers to nonmedical developments important to future Army applications but lacking in commercial incentives. These include investigations in target threat molecules

for battlefield sensors, improved proteins for radiation-resistant electronics, hierarchical design models for advanced combat materials, and interfaces for implanted device substructures.

Conclusion

Potential adversaries are highly likely to take advantage of developments in biotechnology to achieve dubious ends. As such, the Army must position itself to monitor the expanding fields of biotechnology, to influence developments supportive of future applications, and to exploit new opportunities as they appear.

The establishment of a new Army Biotechnology Center, which was proposed after the study was released, will be a major step toward concentrating research and monitoring commercial developments. This new multidisciplinary activity will focus on specific areas of biotechnology with important applicability to the mission needs of future Army forces and with minimal commercial interest and investment.

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